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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/810,243 | 03/19/2001 | Koo Lee | 3275-0107P | 8364 |

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| EXAMINER | |
|---|---|
| LUKTON, DAVID | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | 8 |

DATE MAILED: 10/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/810,243 | LEE ET AL. | |
| | Examiner | Art Unit | |
| | David Lukton | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6-10* is/are rejected.

7)☒ Claim(s) *4 and 5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Pursuant to the directives of paper No. 7 (filed 7/7/03), claim 1 has been amended. Claims 7-10 are joined with the elected group. Claims 1-10 are examined in this Office action.

Applicants' arguments filed 7/7/03 have been considered and found persuasive in part. The rejection over Lumma (*J. Med. Chem.* **41**, 1011 1998) is withdrawn.

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Claims 6-8 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- The dependence of claim 6 on claim 1 is improper. Many of the compounds in claim 6 require "G" to be a carbon atom (bearing hydrogen); this possibility is precluded by claim 1.

- Each of claims 7 and 8 recite the term "trypsin-like". This renders the claims indefinite as to the manner in which, or the extent to which the protease must resemble trypsin in order to qualify as being "trypsin-like".

*

35 U.S.C §101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture or composition of matter or any new and useful improvement therof, may obtain a patent therefore, subject to the conditions and requirements of this title".

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-10 are rejected under 35 USC §101 because the claimed invention is not supported by either an asserted utility or a well established utility.

The cited claims can be viewed as encompassing two categories of embodiment: (a) those in which the mammal is in need of the thrombin inhibitor, and (b) those in which the mammal is not in need of the thrombin inhibitor, and will suffer illness or even death as a result of the administration. It is to this second category that this ground of rejection is targetted. The benefits of thrombin inhibitors to patients suffering excessive thrombosis or platelet aggregation are acknowledged. But for a patient who is afflicted with inadequate thrombosis, a thrombin inhibitor is only going to exacerbate his condition. For example, administering a thrombin inhibitor to a hemophiliac is not going to be very helpful.

This ground of rejection can be overcome by amending claims 7-10 to recite that the mammal is in need of the administration. For example, the following could be used:

> *A method of inhibiting thrombin comprising administering to a mammal in need thereof an effective amount of a compound according to claim 1.*

Claims 7-10 are also rejected under 35 USC §112 first paragraph. Specifically, since the claimed invention is not supported by either an asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

*

Claims 7 and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of claims 7 and 9 assert that one can "modulate" a protease. The term "modulate" would encompass not only inhibition of protease activity, but enhancement of the activity. It is to this second embodiment that this ground of rejection is targeted. The specification provides no guidance to the skilled artisan who is endeavoring to enhance protease activity. The specification only provides guidance as to how to inhibit the activity. The specification is deficient in failing to provide specific process steps that one could take to increase activity of proteases, rather than decreasing it.

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Claims 7 and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Each of claims 7 and 9 assert that one can "modulate" a protease. The term "modulate" would encompass not only inhibition of protease activity, but enhancement of the activity. It is to this second embodiment that this ground of rejection is targeted. The specification

provides no guidance to the skilled artisan who is endeavoring to enhance protease activity. As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. The fact that the compounds are effective to inhibit protease activity supports the conclusion that, for the biochemist who is endeavoring to enhance protease activity, "unpredictable" results will be obtained. There is no evidence that, for a compound which is "active", inhibition can be avoided, and supplanted with enhancement of activity.

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The following is a quotation of the appropriate paragraphs of 35 U.S.C §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2) and (4) of section 371(c) of this title before the invention thereof by the applicant for the patent.

Claims 1-3, 7-10 are rejected under 35 U.S.C. §102(e) as being anticipated by Bohm (USP

6,444,817).

Bohm discloses (col 45, line 65) the following compound:

HOOC-$CH_2$ -(D,L)-Dch-Pro-NH-3-(6-am)-pico

(As disclosed at col 46, line 21, "Dch" represents dicyclohexylalanine).

This is encompassed by claim 1 when the variables are as follows:

A = HOOC-$CH_2$ -
C = cyclohexyl
D = cyclohexyl
E = CH
F = CH
G = N
H = CH
I = amidino

Thus, the claims are anticipated.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

D. Lukton

DAVID LUKTON
PATENT EXAMINER
GROUP 1800